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US-PAT-NO: 7001760

DOCUMENT-IDENTIFIER: US 7001760 B2

TITLE: Hepatitis B virus vectors for gene therapy

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Brief Summary Text - BSTX (14):

The tropism of hepadnaviruses for hepatocytes has particular relevance to the use of HBV in gene therapy for diseases, which are caused by lack of gene expression in liver tissue. These diseases include numerous metabolic diseases, such as hemophilia lacking factor VIII or IX expression in liver. In addition, the HBV vector will be very useful to treat patients with chronic HBV infection. Since most hepatocytes of these chronic patients are equipped with packaging function (i. e., core, polymerase, and surface antigen expression), administration of the vector DNA could lead to **packaging of the recombinant HBV** particles, which could then infect neighboring hepatocytes. Thus, the vector DNA encoding various antiviral functions could induce therapeutic benefit. The vector DNA could be administered via direct intrahepatic injection or via circulation.

Brief Summary Text - BSTX (20):

A few attempts were made to generate recombinant HBV viruses, in which a subset of the HBV genome was substituted by heterologous genes (Chiang et al., 1992; Chaisomchit et al., 1997; Protzer et al., 1999). The present invention significantly differs from reported U.S. Pat. No. 5,981,274 as follows (Chaisomchit, et al., 1997). First of all, a heterologous sequence was inserted into the spacer (or tether) domain of the HBV polymerase ORF as a fusion protein in the patent above. Contrary to this, the present invention indicates that this insertion site overlaps with the .alpha. element found to be essential for the viral genome replication in this invention. Thus, the 50-fold reduction of the viral genome replication as indicated in the patent is a consequence of disruption of the .alpha. element in the vector. Further, the size of insert (267 bp or 374 bp) and its expression as a fusion protein limits its use as a vector. In conclusion, the recombinant HBV vector claimed in the patent above is defective or not capable of **packaging a recombinant HBV** genome encoding a heterologous gene sequence.

Description Paragraph - DETX (5):

FIG. 4. A schematic representation of gene therapy procedure using the hepatitis B virus vector to deliver a heterologous gene (e. g., GFP) to liver cells. A recombinant HBV vector DNA encoding GFP gene is transfected into a packaging cell line that expresses viral proteins necessary for **packaging the recombinant HBV** genome. The produced recombinant HBV particles then infect hepatocytes. Upon the entry of the HBV particles into cells, the viral DNA is repaired to CCC (covalently closed circular) form DNA in the nucleus and

induces the expression of GFP, as the wild-type HBV does. The packaging cell line can be replaced by a helper plasmid that provides core and the viral polymerase.

Other Reference Publication - OREF (4):

Chiang P. et al., Characterization of a cis Element Required for **Packaging and Replication of the Human Hepatitis B** Virus, Virology, 186: 701-11 (1992).
cited by other

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	31635	hepatitis adj "b" or hbv	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2008/01/28 16:18
L2	1270300	encapsulat\$ packag\$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2008/01/28 16:19
L3	88	1 near3 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2008/01/28 16:19
L4	1	2002-019322.NRAN.	DERWENT	OR	OFF	2008/01/28 16:22
L5	0	"0046376".did.	EPO; DERWENT	OR	OFF	2008/01/28 16:44
L6	2	"200046376".did.	EPO; DERWENT	OR	OFF	2008/01/28 16:44
L7	1	2000-514959.NRAN.	DERWENT	OR	OFF	2008/01/28 16:44